NCBI *PubMed* PubMed QUERY PubMed ?

Other Formats: Citation MEDLINE
Links: Related Articles

☐ **Order this document**

Ciba Found Symp 1997;211:160-70; discussion 170-6

Mouse models for the study of telomerase.

Blasco MA, Lee HW, Rizen M, Hanahan D, DePinho R, Greider CW

Department of Immunology and Oncology, Centro Nacional de Biotecnologia, Madrid, Spain.

The ends of chromosomes, or telomeres, consist of short repeated sequences that are synthesized by a ribonucleoprotein-DNA polymerase called telomerase. The RNA component of telomerase is essential for enzyme activity. The maintenance of telomere length by telomerase has been proposed to be essential for cellular viability and to play an important role in cellular senescence and immortalization. We are interested in using the mouse as a model system for the study of telomerase. We studied telomerase activity and expression of the mouse telomerase RNA component (mTR) in two different transgenic mouse models of multistage tumorigenesis: models of islet cell carcinoma and squamous cell carcinoma. In both tumour models, telomerase activity was detected only in late-stage tumours, whereas the telomerase RNA was present at higher than normal levels in pre-neoplastic stages and increased further in late-stage tumours. However, the RNA levels did not parallel the amounts of telomerase activity detected, suggesting that regulation of telomerase activity does not correlate with the regulation of its RNA component. These results establish a direct correlation between progression to late-stage tumours and induction of telomerase activity, and suggest that the initial upregulation of telomerase RNA is an early event. To address the role of telomerase during normal mouse development and tumour formation, we have constructed a knockout mouse for the mouse telomerase RNA, mTR-/-. These mice and the cell lines derived from them are telomerase deficient.

Publication Types:

- Review
- Review, tutorial

PMID: 9524757, UI: 98185445

Genes Cells 1999 Oct;4(10):563-72

Presence of telomeric G-strand tails in the telomerase catalytic subunit TERT knockout mice.

Nikaido R, Haruyama T, Watanabe Y, Iwata H, Iida M, Sugimura H, Yamada N, Ishikawa F

Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama, 226-8501, Japan.

BACKGROUND: Telomerase consists of two essential subunits, the template RNA (TR; telomerase RNA) and the catalytic subunit TERT (telomerase reverse transcriptase). Knockout mice with a mTR (mouse TR) deletion have been described and well characterized. However, mice with a mTERT (mouse TERT) deletion have not been reported. RESULTS: mTERT-knockout mice have been constructed. The first generation mTERT -/- mice were fertile, and did not show any noticeable macroscopic or microscopic phenotypic change. All tissue cells derived from mTERT -/- mice that were examined lacked telomerase activity, indicating that mTERT is the only gene encoding the telomerase catalytic subunit. Pulse field gel electrophoresis (PFGE) and nondenaturing in-gel hybridization analyses showed that mouse telomeric DNA has G-strand 5'-overhangs, as demonstrated for human and yeast cells. This telomeric single-stranded G-tail was also observed in MEF (mouse embryonic fibroblast) and liver cells derived from mTERT -/- mice. CONCLUSIONS: mTERT-knockout mice show phenotypes that are apparently normal at least during the early generations. This observation is similar to that obtained with the mTR-knockout mice. The presence of the telomeric G-strand tails in mTERT -/- mice suggests that these telomeric 5'-overhangs are produced by telomerase-independent mechanisms, as has been proposed for yeast and human.

PMID: 10583505, UI: 20051030

NCBI *PubMed* PubMed QUERY PubMed ?

Other Formats: Citation MEDLINE
Links: Related Articles

☐ Order this document

Genes Cells 1999 Oct;4(10):563-72

Presence of telomeric G-strand tails in the telomerase catalytic subunit TERT knockout mice.

Nikaido R, Haruyama T, Watanabe Y, Iwata H, Iida M, Sugimura H, Yamada N, Ishikawa F

Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama, 226-8501, Japan.

BACKGROUND: Telomerase consists of two essential subunits, the template RNA (TR; telomerase RNA) and the catalytic subunit TERT (telomerase reverse transcriptase). Knockout mice with a mTR (mouse TR) deletion have been described and well characterized. However, mice with a mTERT (mouse TERT) deletion have not been reported. RESULTS: mTERT-knockout mice have been constructed. The first generation mTERT -/- mice were fertile, and did not show any noticeable macroscopic or microscopic phenotypic change. All tissue cells derived from mTERT -/- mice that were examined lacked telomerase activity, indicating that mTERT is the only gene encoding the telomerase catalytic subunit. Pulse field gel electrophoresis (PFGE) and nondenaturing in-gel hybridization analyses showed that mouse telomeric DNA has G-strand 5'-overhangs, as demonstrated for human and yeast cells. This telomeric single-stranded G-tail was also observed in MEF (mouse embryonic fibroblast) and liver cells derived from mTERT -/- mice. CONCLUSIONS: mTERT-knockout mice show phenotypes that are apparently normal at least during the early generations. This observation is similar to that obtained with the mTR-knockout mice. The presence of the telomeric G-strand tails in mTERT -/- mice suggests that these telomeric 5'-overhangs are produced by telomerase-independent mechanisms, as has been proposed for yeast and human.

PMID: 10583505, UI: 20051030